Amendments To The Claims
CLAIMS

1. [Withdrawn] A method for obtaining signature probes comprising the steps of:

A. Compiling a database of nucleic acid sequences from a substantially homologous region of an RNA or DNA comprising sequences from all organisms or viruses that will be incorporated into the analysis;

B. Compiling a bifurcating tree that shows the genetic relationships between the organisms whose nucleic acid sequences will be included in the analysis;

C. Calculating the occurrence frequency and distribution of every oligoribonucleotide or oligodeoxyribonucleotide sequence of length N in the sequence database;

D. Calculating a signature quality function which measures the extent to which each particular oligoribonucleotide or oligodeoxyribonucleotide sequence of length N is characteristic of each node in a substantially bifurcating substantially phylogenetic tree of genetic relationships;

E. Selecting a oligoribonucleotide or oligodeoxyribonucleotide sequences a signature for a particular node if the quality index for said sequence has its greatest value for that node and the quality index exceeds a preset value;

F. Synthesizing signature probes appropriate for use in a hybridization experiment that incorporate the node-specific information of the signature sequences.

2. [Withdrawn] A method of claim 1 in which the signature quality index varies from 0.0 to 1.0 and the preset value is chosen to be greater than 5.

3. [Withdrawn] A method of claim 1 in which the signature quality index Qs is calculated by substantially the equation:

$$Q_s = (N_{GM} / N_{GT}) \times (1 - (N_M - N_{GM}) / N_M)$$
$$= (N_{GM}^2) / (N_{GT} \times N_M)$$

in which where N_M is the number of probe-matched organisms in the entire tree, N_{GM} is the number of probe-matched organisms in the group of interest, and N_{GT} is the number of organisms in the group under consideration.

4. [Currently Amended] ~~1. A method for obtaining signature probes comprising the steps of:~~

~~Compiling a database of nucleic acid sequences from a substantially homologous region of an RNA or DNA comprising sequences from all organisms or viruses that will be incorporated into the analysis;~~

~~Compiling a bifurcating tree that shows the genetic relationships between the organisms whose nucleic acid sequences will be included in the analysis;~~

~~Calculating the occurrence frequency and distribution of every oligoribonucleotide or oligodeoxyribonucleotide sequence of length N in the sequence database;~~

~~Calculating a signature quality function which measures the extent to which each particular oligoribonucleotide or oligodeoxyribonucleotide sequence of length N is characteristic of each node in a substantially bifurcating substantially phylogenetic tree of genetic relationships;~~

~~Selecting a oligoribonucleotide or oligodeoxyribonucleotide sequenceas a signature for a particular node if the quality index for said sequence has its greatest value for that node and the quality index exceeds a preset value;~~

~~Synthesizing signature probes appropriate for use in a hybridization experiment that incorporate the node specific information of the signature sequences.~~

A method of determining the genetic affinity of organisms or viruses in a test sample containing a nucleic acid comprising the steps of:

A. Obtaining or developing a bifurcating node phylogenetic tree that substantially reflects the genetic relationship between the organisms or viruses included in a database of sequences of the nucleic acid.

B. Identifying the extent to which each particular oligonucleotide or sequence of length N is characteristic of each node in the bifurcating node phylogenetic tree of genetic relationship

C. Deriving a plurality of nucleic acid signature probes from a signature- database of signature sequences that are complementary to a portion of the nucleic acid sequence of the organism or virus;

D. Hybridizing the signature probes to the nucleic acid obtained from the test sample under conditions where a detectable signal will be produced by signature probes that hybridize to the nucleic acid of the organism or virus.

E. Identifying signature probes which produce detectable signal;

F. Determining which nodes in the bifurcating node phylogenetic tree of genetic relationship produced detectable signal to identify the closest genetic relatives of the organism or virus in the test sample.

5. [Currently Amended] A method of claim 4 wherein the signature probes are comprised of a moiety selected from the group consisting of: RNA, DNA, an analog of

RNA or DNA including peptide nucleic acids, 2-O-methyl DNA or any other molecule that can interact with the test sample nucleic acid in a sequence-specific way.

6. [Currently Amended] A method of claim 4 wherein the hybridization step utilizes a feature selected from the group consisting of an immobilized array of signature probes, molecular beacons and a hybridization step done in solution.

7. [Original] A method of claim 4 wherein the detection step utilizes radioactive labels, chemiluminescence and/or fluorescence.

8. [Currently Amended] A method of claim 4 wherein ~~a tree of relationships signifying~~ the bifurcating node phylogenetic tree of genetic relationships ~~signifying genetic relationship~~ is generated by ~~a standard method selected from the group consisting of~~ parsimony methods~~, distance methods, and maximum likelihood~~.

9. [Currently Amended] A method of claim 4 wherein the most narrowly defined grouping ~~groupings~~ on the tree of relationship comprises a moiety selected from the group consisting of: a specific genus, a specific species, a race, serotype, type or other grouping below the species level.

10. [Currently Amended] A method of claim 4 in which the ~~signature probes are constructed by the method of claim 1.~~ extent to which each particular oligonucleotide or sequence of length N is characteristic of each node in the tree of genetic relationship is obtained by:

A. Compiling a database of nucleic acid sequences from a substantially homologous RNA or DNA comprising sequences from all organisms or viruses that will be incorporated into the analysis;

B. Calculating the occurrence frequency and distribution of every oligoribonucleotide or oligodeoxyribonucleotide sequence of length N in the sequence data base;

C. Calculating a signature quality function which measures the extent to which each particular oligoribonucleotide or oligodeoxyribonucleotide sequence of length N is characteristic of each node in the bifurcating node phylogenetic tree of genetic relationships.

11. [Withdrawn] A method of devising oligonucleotide probes for use in hybridization comprising using the sequence information provided in a signature sequence to construct the probe.

12. [Withdrawn] An isolated nucleic acid molecule comprising the sequence shown in Table B.

13. [Withdrawn] The RNA sequence CUGCAGAGAUGA or the corresponding DNA sequence, and probes complementary to any of the foregoing or to sequences containing any of the foregoing, which are valuable for identification of samples containing organisms with strong genetic affinity to Legionella nautarum.

14. [Withdrawn] The RNA sequence AAAAUCAUUCUC or the corresponding DNA sequence, and probes complementary to any of the foregoing or to sequences containing any of the foregoing, which are valuable for identification of samples containing organisms with strong genetic affinity to specific for organisms with strong genetic affinity to Listeria gray.

15. [Withdrawn] The RNA sequence CGGGAGGCAGCAGCU or the corresponding DNA sequence, and probes complementary to any of the foregoing or to sequences containing any of the foregoing, which are valuable for identification of samples containing organisms selected from the group of genera consisting of Borrelia, Brachyspira, Spirochaeta and Treponema.

16. [Withdrawn] The RNA sequence AUUACAAACUGU or the corresponding DNA sequence, and probes complementary to any of the foregoing or to sequences containing any of the foregoing,which are valuable for identification of samples containing organisms with strong genetic affinity to Ureaplasma canigenitalium.

17. [Withdrawn] The RNA sequence GGAGGAUGAAGGUUU and GGCGACCUGCUGGAA which are substantially perfect signatures for node 4254 which contains various members of the

genus Helicobacter and GGCGUGCGAGCGUGG which is a substantially perfect signature for node 3634 which contains species of Isosphaera .

18. [Withdrawn] An assay or test kit comprising an RNA sequence selected from the group consisting of AAAAUCAUUCUC, CGGGAGGCAGCAGCU, AUUACAAACUGU, GGAGGAUGAAGGUUU and GGCGACCUGCUGGAA or the corresponding DNA sequence, and probes complementary to any of the foregoing or to sequences containing any of the foregoing.

19. [Currently Amended] A method of claim 4 in which the signature probes are of length 6 or larger and where the nucleic acid is selected from the group consisting of ribosomal RNA, genomic DNA, 10S RNA, RNAse P RNA, guide RNA, telomerase RNA, sn RNAs, scRNAs, and DNA isolated from the spacer region between ribosomal RNA genes or a fragment of the foregoing.

20. [Currently Amended] ~~All inventions contained herein.~~
A method of determining the genetic affinity of organisms or viruses in a test sample comprising detecting the presence of a plurality of signature sequences.

21 [New]A method of claim 4 wherein the hybridization step comprises a feature selected from the group consisting of locked nucleic acids, polymerase chain reaction, RT-PCR, peptide nucleic acids, array detection, and magnetic detection.

22 [New] A method of determining the genetic affinity of organisms or viruses in a test sample containing a nucleic acid comprising the steps of:

A. Obtaining or developing a bifurcating node phylogenetic tree that substantially reflects the genetic relationship between the organisms or viruses included in a database of sequences of the nucleic acid.

B. Identifying the extent to which each particular oligonucleotide or sequence of length N is characteristic of each node in the bifurcating node phylogenetic tree of genetic relationship

C. Deriving a plurality of nucleic acid signature probes from a signature- database of signature sequences that are complementary to a portion of the nucleic acid sequence of the organism or virus;

D. Obtaining a detectable signal for the presence of a signature sequence or its complement in a test sample containing a nucleic acid by utilizing a feature selected from the group consisting of mass spectrometry, polymerase chain reaction, reverse transcription, NASBA amplification, restriction endonuclease digestion, electrophoresis, magnetic detection, and the detection of enzyme activity.

E. Determining which nodes in the bifurcating node phylogenetic tree of genetic relationship produced detectable signal to identify the closest genetic relatives of the organism or virus in the test sample

23 [New] A method of claim 10 in which the signature quality index Qs is calculated by substantially the equation:

$$Q_s = (N_{GM} / N_{GT}) \times (1 - (N_M - N_{GM}) / N_M)$$
$$= (N_{GM}^2) / (N_{GT} \times N_M)$$

in which N_M is the number of probe-matched organisms in the entire tree, N_{GM} is the number of probe-matched organisms in the group of interest, and N_{GT} is the number of organisms in the group under consideration.

24 [New] A method of claim 4 in which the oligonucleotides or sequences of length N comprise genes.

25 [New] A method of Claim 4 in which a set of oligonucleotides or sequences can be used to determine the genetic affinity of at least twice as many organisms or viruses as there are oligonucleotides or sequences in the set.

26 [New] A method of Claim 4 in which a set of not more than 15 oligonucleotides or sequences are used to determine the genetic affinity of at least 18 organisms or viruses.

27 [New] A method of Claim 4 in which the failure to detect a particular oligonucleotide or sequence increases the confidence with which the genetic affinity of an organism or virus is determined.

28 [New] A method of Claim 4 in which the genetic affinity of an organism or virus is determined by an experiment in which at least half the oligonucleotides or sequences tested are not detected, and more than one oligonucleotide or sequence is detected.

29. [New] A method of Claim 10 in which the signature quality function is calculated by a single formula which includes both the presence of sequences in a particular group of organisms or viruses and their presence in other organisms not belonging to that group of organisms or viruses.

30. [New] A method of Claim 4 in which the signature probes used have values of Qs averaging less than 0.95 when calculated by substantially the equation:

$$Q_s = (N_{GM} / N_{GT}) \times (1 - (N_M - N_{GM}) / N_M)$$
$$= (N_{GM}^2) / (N_{GT} \times N_M)$$

in which N_M is the number of probe-matched organisms in the entire tree, N_{GM} is the number of probe-matched organisms in the group of interest, and N_{GT} is the number of organisms in the group under consideration.

31. [New] A method of Claim 4 in which the signature probes used have values of Qs averaging less than 0.85 when calculated by substantially the equation:

$$Q_s = (N_{GM} / N_{GT}) \times (1 - (N_M - N_{GM}) / N_M)$$
$$= (N_{GM}^2) / (N_{GT} \times N_M)$$

in which N_M is the number of probe-matched organisms in the entire tree, N_{GM} is the number of probe-matched organisms in the group of interest, and N_{GT} is the number of organisms in the group under consideration.

32. [New] A method of Claim 4 in which the genetic affinity of an organism or virus not represented in the database is determined.

33. [New] A method of Claim 22 in which the genetic affinity of an organism or virus not represented in the database is determined.

34 [New] The method of claim 20 in which the nucleic acid signature sequences are labeled or chemically modified in their backbone, their sugar, nucleoside base, or any combination thereof.

35 [New] A method of determining the genetic affinity of organisms or viruses in a test sample containing a nucleic acid comprising the steps of:

A) Detecting a signal generated as a result of the presence of a plurality of signature sequences or their complements in the nucleic acid.

B) Comparing a database of the signature sequences found in the nucleic acid to a database of signature sequences found in a plurality of organisms or viruses

C) Determining which Domain, Kingdom, Phylum, Subphylum, Class, Subclass, Order, Suborder, Family, Subfamily, Genus, Species, or Subspecies shares specific genetic affinity with the unknown organism or virus by considering the quality and

number of signal generating signature sequences that are shared with members of each grouping.